REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY (Leave blank)

2. REPORT DATE
8/22/96

3. REPORT TYPE AND DATES COVERED
Final Technical 4/14/93 - 4/14/96

4. TITLE AND SUBTITLE
Mechanisms & Diagnostics of Ultrashort Pulse Laser Ocular Effects

5. FUNDING NUMBERS
F49620-93-1-0301
2312/AS

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8. PERFORMING ORGANIZATION REPORT NUMBER
AFOSR-TR-96
0458

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Air Force Office of Scientific Research
Building 410
Bolling Air Force Base, DC 20332-0001
NL

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES
The view, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other documentation.

12a. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution unlimited.

12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 words)

The objective of our program has been to investigate the mechanisms of short and ultrashort pulse laser retinal injury and to develop and apply new diagnostics for the assessment of retinal injury. A key focus of our effort during this program has been to develop and apply optical coherence tomography (OCT) to investigate the morphology of retinal laser injury. OCT is a new noninvasive optical diagnostic technique for micron scale cross sectional imaging, which can permit the noninvasive imaging of retinal microstructure in situ. Working in collaboration with investigators at Brooks AFB, we have applied OCT to study lesion structure, development, and healing response from laser retinal injury. An increased understanding of the mechanisms of laser retinal injury is relevant to the development of laser safety standards as well as the development and improvement of clinical laser therapies for ocular disease.

DTIC QUALITY INSPECTED 4

14. SUBJECT TERMS

19961016 125

15. NUMBER OF PAGES

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
UNCLASSIFIED	UNCLASSIFIED	UNCLASSIFIED	UL

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

28 AUG 1996

Final Technical Report for the Air Force Office of Scientific Research

Grant No. F49620-93-1-0301

Mechanisms & Diagnostics of Ultrashort Pulse Laser Ocular Effects

April 14, 1993 - April 14, 1996

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2. Objectives

The objective of our program has been to investigate the mechanisms of short and ultrashort pulse laser retinal injury and to develop and apply new diagnostics for the assessment of retinal injury. A key focus of our effort during this program has been to develop and apply optical coherence tomography (OCT) to investigate the morphology of retinal laser injury. OCT is a new noninvasive optical diagnostic technique for micron scale cross sectional imaging, which can permit the noninvasive imaging of retinal microstructure in situ. Working in collaboration with investigators at Brooks AFB, we have applied OCT to study lesion structure, development, and healing response from laser retinal injury. An increased understanding of the mechanisms of laser retinal injury is relevant to the development of laser safety standards as well as the development and improvement of clinical laser therapies for ocular disease.

3. and 4. Status of Effort and Accomplishments / New Findings

Noninvasive Imaging of Retinal Structure using Optical Coherence Tomography

Optical Coherence Tomography is a new medical imaging technique which was developed by our laboratory working in collaboration with MIT Lincoln Laboratory and the New England Eye Center. OCT can perform noninvasive micron scale cross sectional imaging in biological systems. OCT operates in a manner somewhat similar to ultrasound B mode scanning, except that imaging is performed using light rather than sound waves. One of the central components of this program has been the development of OCT technology for the noninvasive imaging of retinal structure and retinal laser lesions. The system that

we developed used 800 nm probe light and achieved an axial resolution of 15 microns.

This technology is enabling for a wide range of investigations ranging from studies of laser retinal injury to the diagnosis and clinical management of retinal diseases.

In-Vivo Imaging of the Evolution of Retinal Laser Lesions using Optical Coherence Tomography

We have performed the first studies which use OCT to image *in vivo* retinal lesions produced by different laser retinal exposure parameters. This investigation was performed in collaboration a multidisciplinary team consisting of investigators from the Armstrong Laboratory at Brooks Air Force Base (specializing in laser retinal injury, safety standards, and veterinary medicine), the Laser Medical Center of Lubeck Germany (specializing in mechanisms of laser injury), and Duke Universiy (clinical ophthalmology). In preliminary studies performed at MIT, we developed an OCT system for retinal tomography and image recording and analysis. This system was transported on site to the Armstrong Laboratory at Brooks Air Force Base where laser exposures were performed.

Laser retinal lesions from several complementary laser sources were investigated. In order to study thermally mediated laser lesions, similar to those used clinically, Argon laser exposures in the 100 ms range were investigated. Short and ultrashort pulse effects were examined using exposures in the nanosecond, picosecond, and femtosecond regime with pulse durations as short as 90 fs. A key advantage of optical coherence tomography is that it permits the *in situ* imaging of retinal lesion morphology in real time. Thus, although OCT does not have as high resolution as histopathology, it can permit repeated imaging of lesions both during their formation and healing.

Studies were performed to image lesions immediately following exposure to track their acute development. In addition, imaging was performed at repeated time intervals post exposure in order to track healing response. Tomographic images of lesions at different time intervals were displayed sequentially to make a movie of lesion development and healing. Retinal images from OCT were also correlated with more conventional endpoints of retinal injury including ophthalmoscopic examination and flourescein angiography. Detailed histological studies were performed on selected lesions and OCT images were correlated with histopathology. This served the dual purpose of giving accurate histopathological information on the lesion morphology as well as defining a baseline for interpreting structures which were observed in OCT images. This study represents was first investigation of retinal injury using OCT and provided the first in vivo view of the microstructure, development, and healing of retinal laser lesions.

Noninvasive Imaging for Cataract Evaluation using OCT

In addition to studies of retinal structure and retinal injury, we have also applied optical coherence tomography for the examination of structures in the anterior eye. Working in collaboration with investigators at the Armstrong Laboratory of Brooks Air Force Base,

we have demonstrated the use of OCT for the noninvasive assessment of cataracts. These studies were performed using geriatric rhesus monkeys from the Brooks Air Force Base Delayed Effects Colony (DEC). Eighteen rhesus monkeys from the DEC and one four year old control rhesus were imaged using OCT, and subsequently evaluated by slit-lamp examination. OCT images were produced and compared to the current and previous cataract grading exams. OCT provided additional information on all opacities (central and peripheral) and provided the information in a log reflective scale format to aid in assessing the extent of the cataract. Studies showed good correlation of OCT images with conventional slit lamp examination and clinical grading of cateracts. In addition OCT provided a detailed map of the structure and morphology for corneal opacities. These studies have the potential for leading to a method for objectively and quantatively assessing cataract progression. Given the prevelance of cataracts, this concept may be of importance for clinical health care management.

5. Personnel Supported and Associated with Effort

Prof. James G. Fujimoto (Professor, Dept. of Electrical Engineering and Computer Science, MIT)

Dr. Brett Bouma (Postdoctoral Associate, Dept. of Electrical Engineering and Computer Science, MIT)

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Collaborators

Dr. William P. Roach (formerly at Armstrong Lab, Brooks AFB, TX)

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Dr. Cheryl D. DiCarlo (formerly at Occupational and Environmental Health Directorate, Brooks AFB, TX)

Dr. Cynthia A. Toth (Professor, Duke Eye Center, Durham, NC)

Dr. Donald A. Gagliano (U.S. Army Medical Research Directorate, Brooks AFB, San Antonio, TX)

Dr. Reginald Birngruber (Director, Medizinisches Laserzentrum, Lubeck, Germany)

Eric A. Swanson (Assistant Group Leader, MIT Lincoln Laboratory, Lexington, MA)

6. Publications

1. J. A. Izatt, M. R. Hee, G. M. Owen, E. A. Swanson, and J. G. Fujimoto, "Optical coherence microscopy in scattering media," *Opt. Lett.* **19**, 590-592, April 1994.

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10. D. G. Narayan, C. A. Toth, S. A. Boppart, M. R. Hee, J. G. Fujimoto, C. P. Cain, C. D. DiCarlo, W. P. Roach, "A comparison of retinal morphology viewed by optical coherence tomography versus light microscopy," in preparation.

7. Interactions / Transitions:

7a. Participation / Presentations at Conferences

1. J. A. Izatt, M. R. Hee, G. Owen, G. Tearney, E. A. Swanson, and J. G. Fujimoto, "Optical coherence microscopy," Advances in Optical Imaging and Photon Migration Topical Meeting, Orlando, FL, March 21-23, 1994, paper WC1.

2. M. R. Hee, J. A. Izatt, D. Huang, E. A. Swanson, C. P. Lin, J. S. Schuman, C. A. Puliafito, and J. G. Fujimoto, "Micron-resolution optical coherence tomography of the human eye," Advances in Optical Imaging and Photon Migration Topical Meeting, Orlando, FL, March 21-23, 1994, paper WA4.

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7. B. Bouma and J. G. Fujimoto, "Nonlinear propagation effects in ultrashort pulse generation," presented at International Workshop on Singularities in Patterns and Collapse: Applications to Semiconductor Lasers and Critical Self-focusing of Ultra-Short Optical Pulses, University College Cork, Cork, Ireland, August 21-26, 1994.

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11. G. J. Tearney, M. R. Hee, J. A. Izatt, B. Bouma, J. G. Fujimoto, M. B. Brezinski, J. F. Southern, R. R. Anderson, and E. A. Swanson, "Optical coherence tomography in multiply scattering tissue," Biomedical Optics Symposium, Photonics West'95, San Jose, CA, February 4-10, 1995, paper 2389-05.

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27. J. G. Fujimoto, "Biomedical imaging with optical coherence tomography," invited paper presented at the Laser Medicine Congress (LASER'95), Munich, Germany, June 19-23, 1995.

28. J. G. Fujimoto, "Biomedical imaging and optical biopsy using optical coherence tomography," invited paper presented at the 15th International Conference on Coherent and Nonlinear Optics (ICONO'95), St. Petersburg, Russia, June 27 - July 1, 1995.

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31. S. A. Boppart, M. E. Brezinksi, B. Bouma, G. J. Tearney, E. A. Swanson, and J. G. Fujimoto, "In vivo imaging of developing morphology using optical coherence tomography," presented at the 1995 American Society of Cell Biology Meeting, Washington, DC, December 9-13, 1995.

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41. J. A. Zuclich, S. T. Schuschereba, H. Zwick, S. A. Boppart, J. G. Fujimoto, F. Cheney, B. E. Stuck, "A comparison of laser-induced retinal damage from 'eye-safe' IR wavelengths to that from visible wavelengths," Oral presentation, Fifth International Congress on Laser Technology in Ophthalmology, Lugano, Switzerland, June 26-29, 1996.

<u>7b and 7c. Consultative and advisory functions / Transitions</u>

(a) Collaborative studies at the Armstrong Laboratory of Brooks Air Force, Optical Radiation Division (Drs. W.P. Roach, B. Rockwell) investigated the structure and evolution of short pulse retinal injury using OCT. Other collaborators included the Occupational and Enviornmental Health Directorate (Dr. Cheryl DiCarlo), TASC (Drs. C. Cain and G. Noojin), Duke Eye Center, University Medical School (Dr. C. Toth) and the Laser Medical Center of Lubeck Germany (Dr. R. Birngruber).

(b) Collaborative studies with the Occupational and Enviornmental Health Directorate (Dr. Cheryl DiCarlo) and the U.S. Army Medical Research Detachment of Brooks AFB (Dr. D. Gagliano) investigated the grading and imaging of cataracts using OCT.

(c) Collaborative studies with 1995 MIT Lincoln Laboratory (E. Swanson) investigated the development of new OCT technology.

(d) Collaborative studies with , the New England Eye Center of the Tufts University School of Medicine (Dr. Carmen Puliafito) investigated the imaging of the normal retina and macular disease in clincal subjects.

8. New discoveries, inventions, patent disclosures

None.

9. Awards, honors

P.I. James G. Fujimoto was General Co-Chair for the Quantum Electronics and Lasers Science Conference, June 1996, Anaheim, CA; Program Co-Chair for the Ultrafast Phenomena conference, May 1996, San Diego, CA; Program Chair for the Optical Imaging and Photon Migration Conference, March 1996, Orlando, FL. He was also elected Fellow of the Optical Society of America (1995) and the IEEE (1995).